)6/16/2009

10/590,976A Yong Chu ·06/14/2008

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| NEWS 2 | JAN 02 | STN pricing information for 2008 now available |
| NEWS 3 | JAN 16 | CAS patent coverage enhanced to include exemplified prophetic substances |
| NEWS 4 | JAN 28 | USPATFULL, USPAT2, and USPATOLD enhanced with new custom IPC display formats |
| NEWS 5 | JAN 28 | MARPAT searching enhanced |
| NEWS 6 | JAN 28 | USGENE now provides USPTO sequence data within 3 days of publication |
| NEWS 7 | JAN 28 | TOXCENTER enhanced with reloaded MEDLINE segment |
| NEWS 8 | JAN 28 | MEDLINE and LMEDLINE reloaded with enhancements |
| NEWS 9 | FEB 08 | STN Express, Version 8.3, now available |
| NEWS 10 | FEB 20 | PCI now available as a replacement to DPCI |
| NEWS 11 | FEB 25 | IFIREF reloaded with enhancements |
| NEWS 12 | FEB 25 | IMSPRODUCT reloaded with enhancements |
| NEWS 13 | FEB 29 | WPINDEX/WPIDS/WPIX enhanced with ECLA and current U.S. National Patent Classification |
| NEWS 14 | MAR 31 | IFICDB, IFIPAT, and IFIUDB enhanced with new custom IPC display formats |
| NEWS 15 | MAR 31 | CAS REGISTRY enhanced with additional experimental spectra |
| NEWS 16 | MAR 31 | CA/CAplus and CASREACT patent number format for U.S. applications updated |
| NEWS 17 | MAR 31 | LPCI now available as a replacement to LDPCI |
| NEWS 18 | MAR 31 | EMBASE, EMBAL, and LEMBASE reloaded with enhancements |
| NEWS 19 | APR 04 | STN AnaVist, Version 1, to be discontinued |
| NEWS 20 | APR 15 | WPIDS, WPINDEX, and WPIX enhanced with new predefined hit display formats |
| NEWS 21 | APR 28 | EMBASE Controlled Term thesaurus enhanced |
| NEWS 22 | APR 28 | IMSRESEARCH reloaded with enhancements |
| NEWS 23 | MAY 30 | INPAFAMDB now available on STN for patent family searching |
| NEWS 24 | MAY 30 | DGENE, PCTGEN, and USGENE enhanced with new homology sequence search option |
| NEWS 25 | JUN 06 | EPFULL enhanced with 260,000 English abstracts |
| NEWS 26 | JUN 06 | KOREAPAT updated with 41,000 documents |
| NEWS 27 | JUN 13 | USPATFULL and USPAT2 updated with 11-character patent numbers for U.S. applications |

NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008

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FILE 'HOME' ENTERED AT 06:50:53 ON 14 JUN 2008

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| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
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| FULL ESTIMATED COST | 0.21 | 0.21 |

FILE 'REGISTRY' ENTERED AT 06:51:11 ON 14 JUN 2008
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STRUCTURE FILE UPDATES:  12 JUN 2008  HIGHEST RN 1027805-40-8
DICTIONARY FILE UPDATES:  12 JUN 2008  HIGHEST RN 1027805-40-8

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http://www.cas.org/support/stngen/stndoc/properties.html

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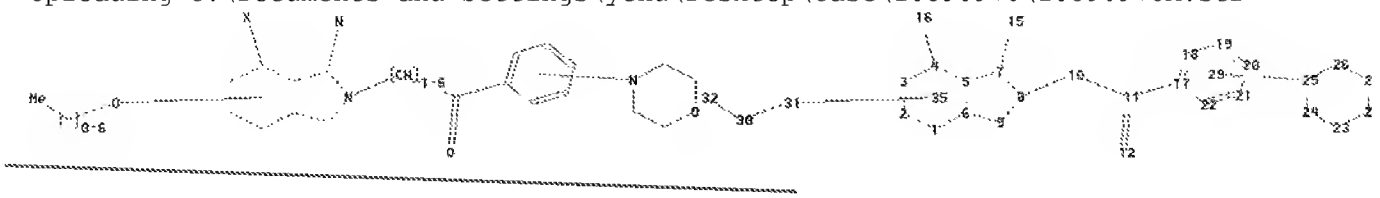
Uploading C:\Documents and Settings\ychu\Desktop\Case\10590976\10590976A.str



chain nodes :
10 11 12 15 16 30 31 32
ring nodes :
1 2 3 4 5 6 7 8 9 17 18 19 20 21 22 23 24 25 26 27 28
chain bonds :

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4-16  7-15  8-10  10-11  11-12  11-17  30-31  30-32
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6  5-7  6-9  7-8  8-9  17-18  17-22  18-19  19-20  20-21
21-22  23-24  23-28  24-25  25-26  26-27  27-28
exact/norm bonds :
1-2  1-6  2-3  3-4  4-5  5-6  5-7  6-9  7-8  7-15  8-9  8-10  11-12  23-24  23-28
24-25  25-26  26-27  27-28  30-31
exact bonds :
4-16  10-11  11-17  30-32
normalized bonds :
17-18  17-22  18-19  19-20  20-21  21-22


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:CLASS
11:CLASS  12:CLASS  15:CLASS  16:CLASS  17:Atom  18:Atom  19:Atom  20:Atom  21:Atom
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35:Atom



L1      STRUCTURE UPLOADED

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L1 HAS NO ANSWERS
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> s l1
SAMPLE SEARCH INITIATED 06:51:43 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -        8 TO ITERATE

100.0% PROCESSED        8 ITERATIONS                                 1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            8 TO      329
PROJECTED ANSWERS:               1 TO       80

L2            1 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 06:51:57 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      150 TO ITERATE

100.0% PROCESSED      150 ITERATIONS                                23 ANSWERS
SEARCH TIME: 00.00.01

L3           23 SEA SSS FUL L1

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COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
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FULL ESTIMATED COST 178.36 178.57

FILE 'CAPLUS' ENTERED AT 06:52:04 ON 14 JUN 2008
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FILE COVERS 1907 - 14 Jun 2008 VOL 148 ISS 25
FILE LAST UPDATED: 13 Jun 2008 (20080613/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
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http://www.cas.org/legal/infopolicy.html

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L4 14 L3

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L4 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:417749 CAPLUS Full-text
DOCUMENT NUMBER: 148:410764
TITLE: Rapidly disintegrating lyophilized oral formulations of a thrombin receptor antagonist for treating acute coronary syndrome
INVENTOR(S): Monteith, David; Veltri, Enrico P.; Duggirala, Srinivas; Falvo, Michael Angelo; Erbey, John R., II; Feng, Kung-i; Pavlovsky, Anastasia; Chawdry, Suliman
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 24pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

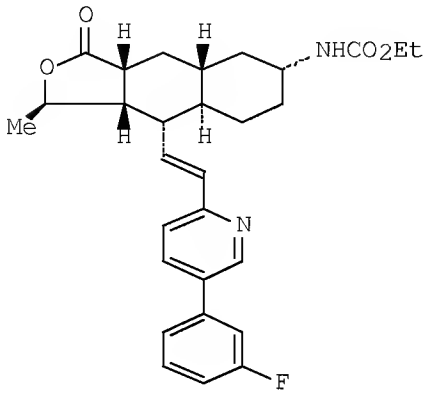
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2008039406 | A2 | 20080403 | WO 2007-US20569 | 20070924 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,

BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2006-847306P P 20060926

GI



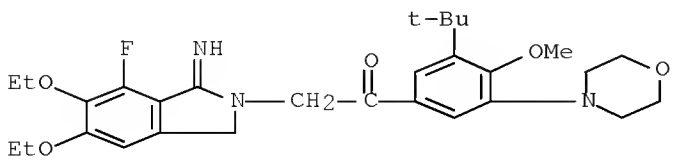
I

AB Disclosed is a lyophilized rapidly disintegrating solid dosage form, one embodiment of which comprises a thrombin receptor antagonist, such as compd. A (I), or a pharmaceutically acceptable salt or hydrate thereof, a polymer such as gelatin, and a matrix forming agent such as mannitol. Systems for effectively buffering the pre-lyophilized suspension are taught, along with methods of treating patients at risk for acute coronary syndrome by administering such a rapidly disintegrating solid dosage form. Thus, a lyophilized formulation comprised (in wt% prior to lyophilization): compd. A bisulfate 8, gelatin 3.5, mannitol 3, flavor (spearmint or peppermint) 0.5, aspartame 0.5, 10% NaOH 4, purified water q.s. to 100 mL.

IT 751475-53-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rapidly disintegrating lyophilized oral formulations of a thrombin receptor antagonist for treating acute coronary syndrome)

RN 751475-53-3 CAPLUS

CN Ethanone, 2-(5,6-diethoxy-7-fluoro-1,3-dihydro-1-imino-2H-isoindol-2-yl)-1-[3-(1,1-dimethylethyl)-4-methoxy-5-(4-morpholinyl)phenyl]- (CA INDEX NAME)



L4 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2008:43916 CAPLUS Full-text

DOCUMENT NUMBER: 148:106256

TITLE: Solid dose formulations of a thrombin receptor

antagonist for treatment of vascular disorders

INVENTOR(S): Gupta, Rajan; Sangekar, Surenda
PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 22pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2008005352 | A2 | 20080110 | WO 2007-US15167 | 20070629 |
| WO 2008005352 | A3 | 20080410 | | |

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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

| | | | | |
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| US 20080026050 | A1 | 20080131 | US 2007-771571 | 20070629 |

PRIORITY APPLN. INFO.: US 2006-817820P P 20060630

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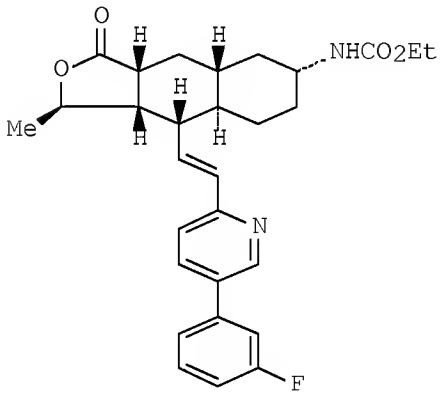



I

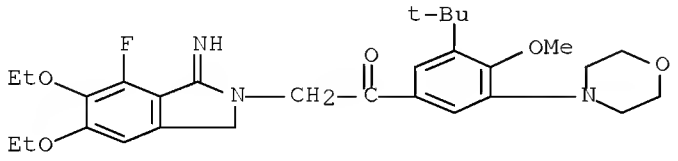
AB Capsule formulations of a thrombin receptor antagonist for oral administration in treatment of vascular disorders are disclosed. In some embodiments, the thrombin receptor antagonist is compd. of formula (I), or a pharmaceutically acceptable isomer, salt, or solvate thereof. The formulations include at least one excipient, such as a diluent, disintegrant and/or lubricant. Also disclosed are methods of treating acute coronary syndrome and peripheral arterial disease, and of effecting secondary prevention, by orally administering such capsule formulations. Thus, a capsule formulation contained

compd. I 0.25 mg, microcryst. cellulose PH101 140.75 mg, crospovidone 7.5, magnesium stearate 1.5 mg.

IT 751475-53-3, E 5555
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(capsules of thrombin receptor antagonist for treatment of vascular disorders)

RN 751475-53-3 CAPLUS

CN Ethanone, 2-(5,6-diethoxy-7-fluoro-1,3-dihydro-1-imino-2H-isoindol-2-yl)-1-[3-(1,1-dimethylethyl)-4-methoxy-5-(4-morpholinyl)phenyl]- (CA INDEX NAME)




L4 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2008:42838 CAPLUS Full-text

DOCUMENT NUMBER: 148:106251

TITLE: Immediate-release tablet formulations of a thrombin receptor antagonist

INVENTOR(S): Gupta, Rajan; Chawdry, Suliman; Duggirala, Srinivas S.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 34pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2008005353 | A2 | 20080110 | WO 2007-US15168 | 20070629 |
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| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| US 20080031943 | A1 | 20080207 | US 2007-771520 | 20070629 |

PRIORITY APPLN. INFO.: US 2006-817821P P 20060630

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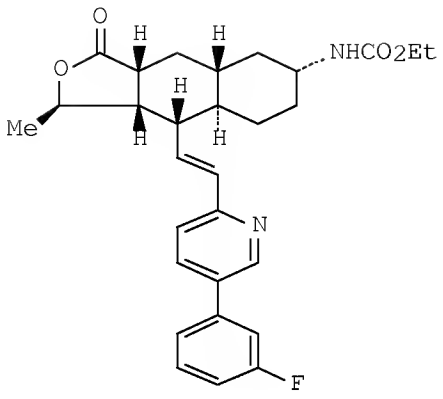


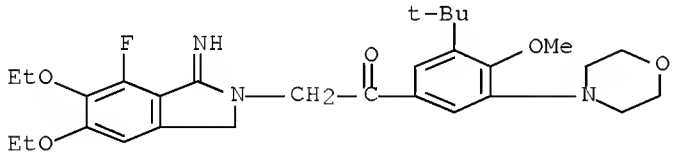
I

AB Immediate-release formulations for oral administration of a thrombin receptor antagonist in treatment of vascular disorders are provided. Certain formulations of higher active pharmaceutical ingredient (API) loading demonstrate sufficient moisture uptake after storage at stressed conditions to retard dissoln. The formulations of the present invention incorporate either lower API loading or elevated disintegrant-to-API ratios, found necessary to achieve disintegration rates required for immediate-release performance. Thus, a tablet formulation contained compd. I bisulfate 40 mg, lactose monohydrate 383 mg, microcryst. cellulose 120 mg, croscarmellose sodium 36 mg, Povidone 18 mg, and magnesium stearate 3 mg.

IT 751475-53-3, E 5555
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immediate-release tablets of thrombin receptor antagonist for treatment of vascular disorders)

RN 751475-53-3 CAPLUS

CN Ethanone, 2-(5,6-diethoxy-7-fluoro-1,3-dihydro-1-imino-2H-isoindol-2-yl)-1-[3-(1,1-dimethylethyl)-4-methoxy-5-(4-morpholinyl)phenyl]- (CA INDEX NAME)



L4 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1177798 CAPLUS Full-text

DOCUMENT NUMBER: 147:440330

TITLE: Use of combination of thrombin receptor antagonists and cardiovascular agents for the treatment of cardiovascular disorders

INVENTOR(S): Veltri, Enrico P.; Greenlee, William J.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 33pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2007117621 | A1 | 20071018 | WO 2007-US8612 | 20070405 |

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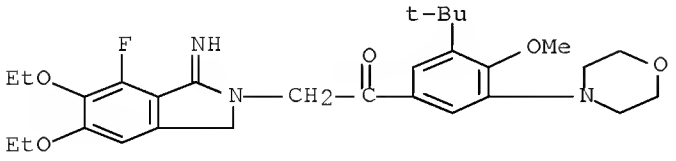
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

| PRIORITY APPLN. INFO.: | | |
|---|---|---|
| US 2006-790469P | P | 20060406 |
| US 2006-808611P | P | 20060526 |
| US 2006-809785P | P | 20060531 |
| US 2006-839474P | P | 20060823 |
| US 2006-839484P | P | 20060823 |

AB Disclosed herein are pharmaceutical combinations comprising at least one thrombin receptor antagonist and at least one cardiovascular agent. The thrombin receptor antagonists are statins or antiarrhythmic agents and cardiovascular agents suitable for co-formulation or co-administration with the thrombin receptor antagonist include an endothelin antagonist selected from the group consisting of tezosentan, bosentan, and sitaxsentan (no data).

IT 751475-53-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of combination of thrombin receptor antagonists and cardiovascular agents for treatment of cardiovascular disorders)

RN 751475-53-3 CAPLUS
CN Ethanone, 2-(5,6-diethoxy-7-fluoro-1,3-dihydro-1-imino-2H-isoindol-2-yl)-1-[3-(1,1-dimethylethyl)-4-methoxy-5-(4-morpholinyl)phenyl]- (CA INDEX NAME)




REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1150265 CAPLUS Full-text
DOCUMENT NUMBER: 147:433639
TITLE: Composition comprising thrombin receptor antagonist and cardiovascular agent
INVENTOR(S): Veltri, Enrico P.; Greenlee, William J.
PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 13pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
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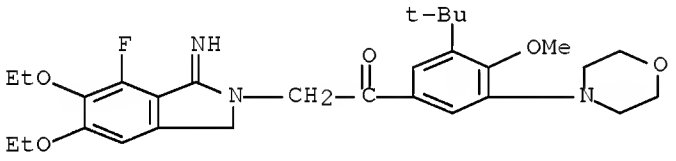
| US 20070238674 | A1 | 20071011 | US 2007-696898 | | 20070405 |
| PRIORITY APPLN. INFO.: | | | US 2006-790469P | P | 20060406 |
| | | | US 2006-808611P | P | 20060526 |
| | | | US 2006-809785P | P | 20060531 |
| | | | US 2006-839474P | P | 20060823 |
| | | | US 2006-839484P | P | 20060823 |
| | | | US 2007-887236P | P | 20070130 |

AB This invention relates to pharmaceutical combinations comprising at least one thrombin receptor antagonist and at least one cardiovascular agent.

IT 751475-53-3, E 5555
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(E 5555; compn. comprising thrombin receptor antagonist and cardiovascular agent)

RN 751475-53-3 CAPLUS

CN Ethanone, 2-(5,6-diethoxy-7-fluoro-1,3-dihydro-1-imino-2H-isoindol-2-yl)-1-[3-(1,1-dimethylethyl)-4-methoxy-5-(4-morpholinyl)phenyl]- (CA INDEX NAME)




L4 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1028574 CAPLUS Full-text
DOCUMENT NUMBER: 147:336290
TITLE: Method for determination of the effect of thrombin receptor antagonist by determination of inflammatory marker
INVENTOR(S): Kogushi, Motoji; Yokohama, Hiromitsu; Kitamura, Shinichi
PATENT ASSIGNEE(S): Eisai R & D Management Co., Ltd., Japan
SOURCE: PCT Int. Appl., 40pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2007102563 | A1 | 20070913 | WO 2007-JP54490 | 20070301 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, | | | | |

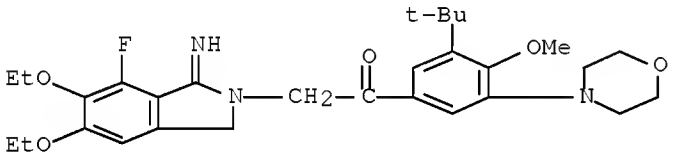
KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN,
MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS,
RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,
GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: JP 2006-56255 A 20060302
OTHER SOURCE(S): MARPAT 147:336290

AB Disclosed is a method for detn. of the inhibitory effect of a thrombin receptor antagonist on the occurrence of a cardiovascular event, based on the results obtained by the detn. of an inflammatory marker in a biol. sample.

IT 751475-53-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for detn. of the effect of thrombin receptor antagonist by detn. of inflammatory marker)

RN 751475-53-3 CAPLUS
CN Ethanone, 2-(5,6-diethoxy-7-fluoro-1,3-dihydro-1-imino-2H-isoindol-2-yl)-1-[3-(1,1-dimethylethyl)-4-methoxy-5-(4-morpholinyl)phenyl]- (CA INDEX NAME)




REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:730904 CAPLUS Full-text
DOCUMENT NUMBER: 147:125616
TITLE: Thrombin receptor antagonists as prophylaxis to complications from cardiopulmonary surgery
INVENTOR(S): Veltri, Enrico P.; Strony, John T.; Berman, Gail
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 31pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2007075964 | A2 | 20070705 | WO 2006-US48928 | 20061220 |
| WO 2007075964 | A3 | 20070920 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN,
KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK,
MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO,

RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

| | | | | |
|---|---|---|---|---|
| US 20070202140 | A1 | 20070830 | US 2006-613450 | 20061220 |
| PRIORITY APPLN. INFO.: | | | US 2005-753246P | P 20051222 |

GI

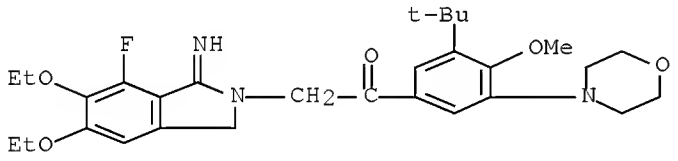
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Methods are provided for preventing, inhibiting, or ameliorating complications assocd. with cardiopulmonary bypass surgery, such as bleeding, thrombotic vascular events, graft failure, atherosclerosis, angina pectoris, myocardial ischemia, etc., by the use of a thrombin receptor antagonist. Examples of such thrombin receptor antagonists include I, II, and III. The method further comprises administering at least one cardiovascular agent selected from the group consisting of thromboxane A2 biosynthesis inhibitors, thromboxane antagonists, ADP inhibitors, cyclooxygenase inhibitors, angiotensin antagonists, endothelin antagonists, phosphodiesterase inhibitors, angiotensin converting enzyme inhibitors, neutral endopeptidase inhibitors, anticoagulants, diuretics, platelet aggregation inhibitors; and GP IIb/IIIa antagonists.

IT 751475-53-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thrombin receptor antagonists in combination with cardiovascular agents as prophylaxis to complications from cardiopulmonary surgery)

RN 751475-53-3 CAPLUS

CN Ethanone, 2-(5,6-diethoxy-7-fluoro-1,3-dihydro-1-imino-2H-isoindol-2-yl)-1-[3-(1,1-dimethylethyl)-4-methoxy-5-(4-morpholinyl)phenyl]- (CA INDEX NAME)




L4 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN

| | |
|---|---|
| ACCESSION NUMBER: | 2006:470154 CAPLUS Full-text |
| DOCUMENT NUMBER: | 144:460841 |
| TITLE: | Remedy for angiospasm accompanying subarachnoid hemorrhage containing thrombin receptor antagonist as the active ingredient |
| INVENTOR(S): | Hirano, Katsuya; Maeda, Yoshihisa; Sasaki, Tomio; Kanaide, Hideo; Kai, Yasutoshi |
| PATENT ASSIGNEE(S): | Eisai Co., Ltd., Japan; Kyushu University, National University Corporation |
| SOURCE: | PCT Int. Appl., 63 pp.<br>CODEN: PIXXD2 |

DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006051648 | A1 | 20060518 | WO 2005-JP16568 | 20050902 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| WO 2006051623 | A1 | 20060518 | WO 2005-JP5068 | 20050315 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| EP 1813282 | A1 | 20070801 | EP 2005-782159 | 20050902 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU | | | | |
| JP 2007084440 | A | 20070405 | JP 2005-268246 | 20050915 |

| | | | |
|---|---|---|---|
| PRIORITY APPLN. INFO.: | US 2004-626412P | P | 20041109 |
| | WO 2005-JP5068 | A | 20050315 |
| | JP 2006-529356 | A | 20050315 |
| | WO 2005-JP16568 | W | 20050902 |

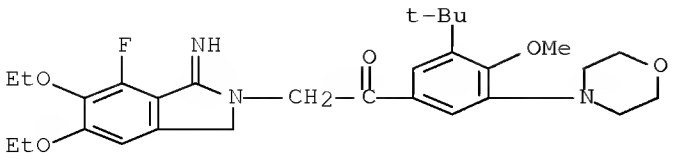
OTHER SOURCE(S): MARPAT 144:460841

AB A remedy for subarachnoid hemorrhage or a drug for improving prognosis of subarachnoid hemorrhage which contains a compd. having a PAR1 inhibitory effect, its pharmaceutically acceptable salt or a hydrate of the same.

IT 751475-53-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(2-iminopyrrolidine derivs. as thrombin receptor antagonists for treatment of angiospasm accompanying subarachnoid hemorrhage)

RN 751475-53-3 CAPLUS

CN Ethanone, 2-(5,6-diethoxy-7-fluoro-1,3-dihydro-1-imino-2H-isoindol-2-yl)-1-[3-(1,1-dimethylethyl)-4-methoxy-5-(4-morpholinyl)phenyl]- (CA INDEX NAME)




REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:469727 CAPLUS Full-text
DOCUMENT NUMBER: 144:445366
TITLE: Therapeutic agent for angiospasm caused by subarachnoid hemorrhage, containing thrombin receptor antagonist as active ingredient
INVENTOR(S): Hirano, Katsuya; Maeda, Yoshihisa; Sasaki, Tomio; Kanaide, Hideo; Kai, Yasutoshi
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan; Kyushu University, National University Corporation
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006051623 | A1 | 20060518 | WO 2005-JP5068 | 20050315 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| WO 2006051648 | A1 | 20060518 | WO 2005-JP16568 | 20050902 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| EP 1813282 | A1 | 20070801 | EP 2005-782159 | 20050902 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU | | | | |

JP 2007084440 A 20070405 JP 2005-268246 20050915
PRIORITY APPLN. INFO.: US 2004-626412P P 20041109
JP 2006-529356 A 20050315
WO 2005-JP5068 A 20050315
WO 2005-JP16568 W 20050902

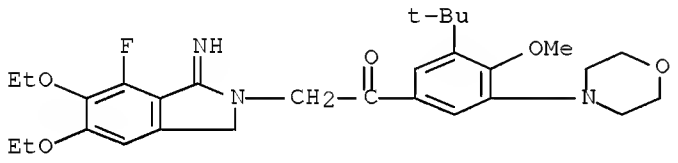
OTHER SOURCE(S): MARPAT 144:445366

AB A therapeutic agent for subarachnoid hemorrhage, or prognosis improving agent for subarachnoid hemorrhage, comprising a compd. having PAR1 inhibiting potency, or its pharmacol. acceptable salt, or a hydrate thereof.

IT 751475-53-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic agent for angiospasm caused by subarachnoid hemorrhage, contg. 2-iminopyrrolidine deriv. as thrombin receptor antagonist as active ingredient)

RN 751475-53-3 CAPLUS

CN Ethanone, 2-(5,6-diethoxy-7-fluoro-1,3-dihydro-1-imino-2H-isoindol-2-yl)-1-[3-(1,1-dimethylethyl)-4-methoxy-5-(4-morpholinyl)phenyl]- (CA INDEX NAME)




REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:230936 CAPLUS Full-text
DOCUMENT NUMBER: 144:311793
TITLE: Processes for producing fluorinated cyclic benzamidine derivative
INVENTOR(S): Shimomura, Naoyuki; Sasho, Manabu; Kayano, Akio; Yoshizawa, Kazuhiro; Tsujii, Masahiko; Kuroda, Hiroshi; Furukawa, Ken
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: U.S. Pat. Appl. Publ., 38 pp., Cont.-in-part of Appl. No. PCT/JP04/001396.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 20060058370 | A1 | 20060316 | US 2005-208289 | 20050818 |
| US 7375236 | B2 | 20080520 | | |
| WO 2004078721 | A1 | 20040916 | WO 2004-JP1396 | 20040210 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,

BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2003-40949 A 20030219
WO 2004-JP1396 A2 20040210

OTHER SOURCE(S): CASREACT 144:311793; MARPAT 144:311793

GI

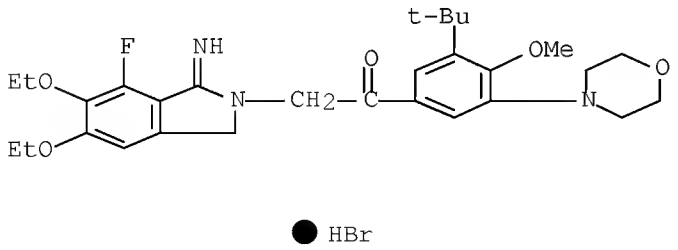
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A process for producing fluorinated cyclic benzamidine derivs. (I), (II) or salt thereof, characterized by comprising the step of reacting compd. (III) [X = leaving group] with ammonia or an imide; a process for producing a morpholine-substituted phenacyl deriv. (IV) or salt thereof, characterized by comprising reacting a specific compd. with morpholine, reacting the reaction product with a halogenating reagent, and subjecting the resultant reaction product to a reaction for ketal elimination; a process for producing a cyclic benzamidine deriv. (V) or salt thereof, characterized by coupling the compd. I, II or salt with the compd. IV or salt in the presence of an ether or hydrocarbon; and a method of recrystg. the cyclic benzamidine deriv. V or salt, characterized by dissolving the compd. V or salt in a mixed solvent comprising an alc. and water or in a mixed solvent comprising an ether and water and adding water to the soln. to ppt. crystals of the compd. V or salt was disclosed. For example, to a soln. of compd. IV (550 g) in THF (3 L) was added a soln. of compd. I (300 g) in THF (4.5 L) portionwise at 6 .degree.C . Addnl. stirring for 18 h followed by crystn. with 50% THF/water (5 L) afforded compd. V.cntdot.HBr (622.1 g).

IT 474550-69-1P
RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(crystal structure; prepn. and crystal structure of fluorinated cyclic benzamidine deriv.)

RN 474550-69-1 CAPLUS

CN Ethanone, 2-(5,6-diethoxy-7-fluoro-1,3-dihydro-1-imino-2H-isoindol-2-yl)-1-[3-(1,1-dimethylethyl)-4-methoxy-5-(4-morpholinyl)phenyl]-, hydrobromide (1:1) (CA INDEX NAME)

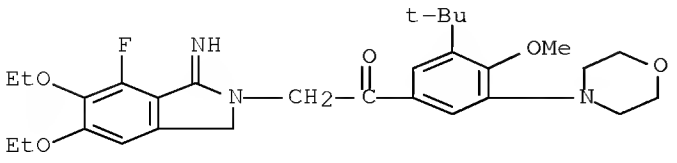



IT 751475-53-3P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and crystal structure of fluorinated cyclic benzamidine deriv.)

RN 751475-53-3 CAPLUS

CN Ethanone, 2-(5,6-diethoxy-7-fluoro-1,3-dihydro-1-imino-2H-isoindol-2-yl)-1-

[3-(1,1-dimethylethyl)-4-methoxy-5-(4-morpholinyl)phenyl]- (CA INDEX NAME)

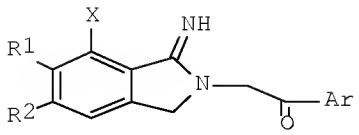



L4 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1004569 CAPLUS Full-text
DOCUMENT NUMBER: 143:292577
TITLE: Composition containing benzamidine derivative and method for stabilizing benzamidine derivative
INVENTOR(S): Suzuki, Yasuyuki; Fujioka, Satoshi
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005084679 | A1 | 20050915 | WO 2005-JP3742 | 20050304 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2005219090 | A1 | 20050915 | AU 2005-219090 | 20050304 |
| AU 2005219090 | B2 | 20080110 | | |
| CA 2558191 | A1 | 20050915 | CA 2005-2558191 | 20050304 |
| EP 1721610 | A1 | 20061115 | EP 2005-720014 | 20050304 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU | | | | |
| CN 1925861 | A | 20070307 | CN 2005-80006933 | 20050304 |
| US 20070208016 | A1 | 20070906 | US 2006-590976 | 20060828 |
| KR 760448 | B1 | 20071004 | KR 2006-717795 | 20060901 |

PRIORITY APPLN. INFO.: JP 2004-61472 A 20040304
WO 2005-JP3742 W 20050304

OTHER SOURCE(S): MARPAT 143:292577
GI



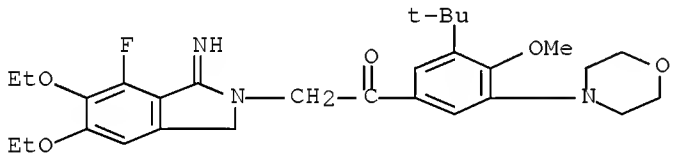
I

AB Disclosed is a compn. contg. a benzamidine deriv. which is not decompd. even under humidified conditions. Also disclosed is a method for stabilizing a benzamidine deriv. Decompn. reaction of benzamidine derivs. can be suppressed by adding at least one electrolyte selected from the group consisting of halide salts of alkali metals or alk. earth metals and perchlorates of alkali metals or alk. earth metals to a benzamidine deriv. represented by the general formula I (R1, R2 = H, methoxy, ethoxy; X = H, halogen; Ar = Me, Et, methoxy, ethoxy, tert-Bu, morpholinyl, etc), or a pharmacol. acceptable salt thereof. For example, tablets were prepd. from 1-(3-tert-butyl-4-methoxy-5-morpholino-phenyl)-2-(5,6-diethoxy-7-fluoro-1- imino-1,3-dihydro-isoindol-2-yl)-ethanone 1, lactose 117, hydroxypropyl cellulose 7.5, hydroxypropyl Me cellulose 4.5, NaCl 4.5, cryst. cellulose 15, and magnesium stearate 0.75 g.

IT 751475-53-3
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. contg. benzamidine derivs. and electrolytes, and method for stabilizing benzamidine deriv.)

RN 751475-53-3 CAPLUS

CN Ethanone, 2-(5,6-diethoxy-7-fluoro-1,3-dihydro-1-imino-2H-isoindol-2-yl)-1-[3-(1,1-dimethylethyl)-4-methoxy-5-(4-morpholinyl)phenyl]- (CA INDEX NAME)




REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1003563 CAPLUS Full-text
DOCUMENT NUMBER: 143:312129
TITLE: Method for preparation of material for drug compatibility test, and test kit having the material
INVENTOR(S): Watanabe, Reiko; Suzuki, Yasuyuki
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 15 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 2005249570 | A | 20050915 | JP 2004-60204 | 20040304 |

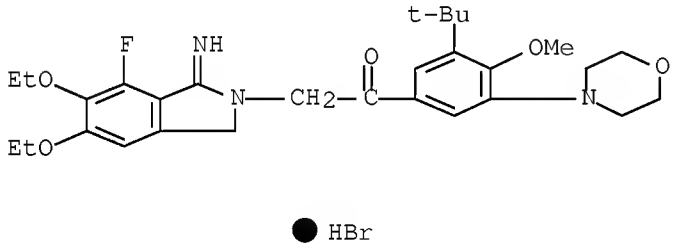
PRIORITY APPLN. INFO.: JP 2004-60204 20040304

AB The invention relates to a method for prepn. of a material for efficient test for examg. compatibility of a drug with other drugs, excipients, and packaging materials, etc., wherein the method include forming a soln./dispersion of each substance, applying the soln./dispersion to a container, e.g. a microplate, and freeze-dried the container. For example, solns./water dispersions of D-mannitol, lactose, anhyd. calcium phosphate, cryst. cellulose, corn starch, hydroxypropyl cellulose, povidone, low-substituted hydroxypropyl cellulose, cross-povidone, croscarmellose sodium were prepd., and applied to a 96 well microplate with various combinations. The microplate was then freeze-dried to obtain a drug compatibility test kit. A soln. of a test substance contg. 1-(3-tert-butyl-4-methoxy-5-morpholinophenyl)-2-(5,6-diethoxy-7-fluoro-1- imino-1,3-dihydro-2H-isoindol-2-yl)ethanone hydrobromide was applied to each wells of the microplate and freeze-dried for further process for HPLC anal.

IT 474550-69-1
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(method for prepn. of material for drug compatibility test, and test kit having the material)

RN 474550-69-1 CAPLUS

CN Ethanone, 2-(5,6-diethoxy-7-fluoro-1,3-dihydro-1-imino-2H-isoindol-2-yl)-1-[3-(1,1-dimethylethyl)-4-methoxy-5-(4-morpholinyl)phenyl]-, hydrobromide (1:1) (CA INDEX NAME)




L4 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:756689 CAPLUS Full-text

DOCUMENT NUMBER: 141:260409

TITLE: Processes for producing fluorinated cyclic benzamidine derivative

INVENTOR(S): Shimomura, Naoyuki; Sasho, Manabu; Kayano, Akio; Yoshizawa, Kazuhiro; Tsujii, Masahiko; Kuroda, Hiroshi; Furukawa, Ken

PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan

SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

| | | | | | |
|---|---|---|---|---|---|
| WO 2004078721 | A1 | 20040916 | WO 2004-JP1396 | | 20040210 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI | | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | | |
| AU 2004218187 | A1 | 20040916 | AU 2004-218187 | | 20040210 |
| CA 2515715 | A1 | 20040916 | CA 2004-2515715 | | 20040210 |
| EP 1602646 | A1 | 20051207 | EP 2004-709710 | | 20040210 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | | |
| CN 1777583 | A | 20060524 | CN 2004-80010500 | | 20040210 |
| US 20060058370 | A1 | 20060316 | US 2005-208289 | | 20050818 |
| US 7375236 | B2 | 20080520 | | | |
| IN 2007CN02019 | A | 20080404 | IN 2007-CN2019 | | 20070511 |
| PRIORITY APPLN. INFO.: | | | JP 2003-40949 | A | 20030219 |
| | | | IN 2005-CN2311 | A3 | 20040210 |
| | | | WO 2004-JP1396 | A | 20040210 |

OTHER SOURCE(S): MARPAT 141:260409
GI

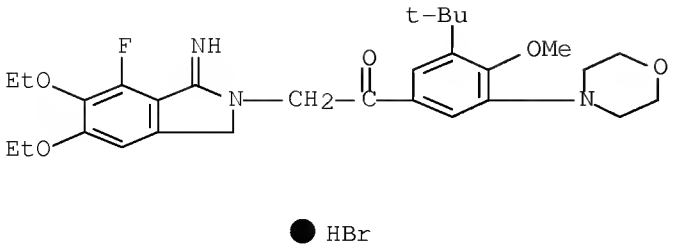

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *


AB A process for producing fluorinated cyclic benzamidine derivs. I, II or salt thereof, characterized by comprising the step of reacting compd. III [X = leaving group] with ammonia or an imide; a process for producing a morpholine-substituted phenacyl deriv. IV or salt thereof, characterized by comprising reacting a specific compd. with morpholine, reacting the reaction product with a halogenating reagent, and subjecting the resultant reaction product to a reaction for ketal elimination; a process for producing a cyclic benzamidine deriv. V or salt thereof, characterized by coupling the compd. I, II or salt with the compd. IV or salt in the presence of an ether or hydrocarbon; and a method of recrystg. the cyclic benzamidine deriv. V or salt, characterized by dissolving the compd. V or salt in a mixed solvent comprising an alc. and water or in a mixed solvent comprising an ether and water and adding water to the soln. to ppt. crystals of the compd. V or salt was disclosed. For example, to a soln. of compd. IV (550 g) in THF (3 L) was added a soln. of compd. I (300 g) in THF (4.5 L) portionwise at 6 .degree.C . Addnl. stirring for 18 h followed by crystn. with 50% THF/water (5 L) afforded compd. V.cntdot.HBr (622.1 g).


IT 474550-69-1P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (crystal structure; prepn. and crystal structure of fluorinated cyclic benzamidine deriv.)

RN 474550-69-1 CAPLUS

CN Ethanone, 2-(5,6-diethoxy-7-fluoro-1,3-dihydro-1-imino-2H-isoindol-2-yl)-1-[3-(1,1-dimethylethyl)-4-methoxy-5-(4-morpholinyl)phenyl]-, hydrobromide (1:1) (CA INDEX NAME)




REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

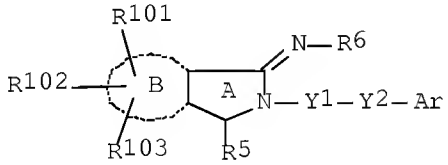
L4 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:832759 CAPLUS Full-text
DOCUMENT NUMBER: 137:353062
TITLE: Preparation of 2-iminopyrrolidine derivatives as thrombin receptor antagonists
INVENTOR(S): Suzuki, Shuichi; Kotake, Makoto; Miyamoto, Mitsuaki; Kawahara, Tetsuya; Kajiwara, Akiharu; Hishinuma, Ieharu; Okano, Kazuo; Miyazawa, Syuhei; Clark, Richard; Ozaki, Fumihiro; Sato, Nobuaki; Shinoda, Masanobu; Kamada, Atsushi; Tsukada, Itaru; Matsuura, Fumiyoshi; Naoe, Yoshimitsu; Terauchi, Taro; Oohashi, Yoshiaki; Ito, Osamu; Tanaka, Hiroshi; Musya, Takashi; Kogushi, Motoji; Kawada, Tsutomu; Matsuoka, Toshiyuki; Kobayashi, Hiroko; Chiba, Kenichi; Kimura, Akifumi; Ono, Naoto
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: PCT Int. Appl., 948 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002085855 | A1 | 20021031 | WO 2002-JP3961 | 20020419 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2446924 | A1 | 20021031 | CA 2002-2446924 | 20020419 |
| AU 2002255269 | A1 | 20021105 | AU 2002-255269 | 20020419 |
| AU 2002255269 | B2 | 20070315 | | |
| EP 1391451 | A1 | 20040225 | EP 2002-724628 | 20020419 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| BR 2002008985 | A | 20040309 | BR 2002-8985 | 20020419 |
| CN 1503784 | A | 20040609 | CN 2002-808565 | 20020419 |
| HU 2004000467 | A2 | 20050228 | HU 2004-467 | 20020419 |

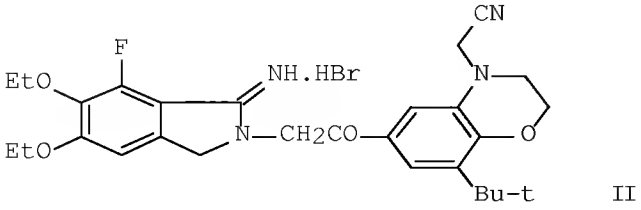
| | | | | |
|---|---|---|---|---|
| EP 1614680 | A2 | 20060111 | EP 2005-22069 | 20020419 |
| EP 1614680 | A3 | 20060201 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR | | | | |
| CN 1733725 | A | 20060215 | CN 2005-10080404 | 20020419 |
| RU 2270192 | C2 | 20060220 | RU 2003-133664 | 20020419 |
| CN 1754880 | A | 20060405 | CN 2005-10080403 | 20020419 |
| JP 3795458 | B2 | 20060712 | JP 2002-583382 | 20020419 |
| NZ 528820 | A | 20070126 | NZ 2002-528820 | 20020419 |
| NO 2003004632 | A | 20031219 | NO 2003-4632 | 20031016 |
| MX 2003PA09497 | A | 20040524 | MX 2003-PA9497 | 20031016 |
| ZA 2003008064 | A | 20050207 | ZA 2003-8064 | 20031016 |
| KR 749794 | B1 | 20070817 | KR 2003-713674 | 20031018 |
| IN 2003DN01719 | A | 20051014 | IN 2003-DN1719 | 20031020 |
| US 20050004204 | A1 | 20050106 | US 2004-475188 | 20040609 |
| US 7244730 | B2 | 20070717 | | |
| AU 2005202135 | A1 | 20050609 | AU 2005-202135 | 20050517 |
| AU 2005202135 | B2 | 20071115 | | |
| KR 749795 | B1 | 20070817 | KR 2005-709505 | 20050526 |
| US 20050245592 | A1 | 20051103 | US 2005-158941 | 20050622 |
| JP 2006206595 | A | 20060810 | JP 2006-41270 | 20060217 |
| JP 2006225393 | A | 20060831 | JP 2006-41255 | 20060217 |
| PRIORITY APPLN. INFO.: | | | JP 2001-121829 | A 20010419 |
| | | | JP 2001-269422 | A 20010905 |
| | | | AU 2002-255269 | A3 20020419 |
| | | | CN 2002-808565 | A3 20020419 |
| | | | EP 2002-724628 | A3 20020419 |
| | | | JP 2002-583382 | A3 20020419 |
| | | | WO 2002-JP3961 | W 20020419 |
| | | | KR 2003-713674 | A3 20031018 |
| | | | US 2004-475188 | A1 20040609 |

OTHER SOURCE(S): MARPAT 137:353062

GI




I



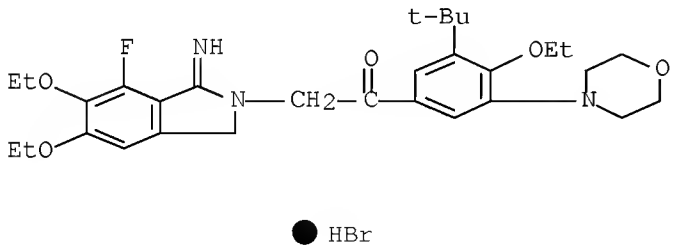

II

AB 2-Iminopyrrolidine derivs. including 2,3-dihydro-1H-isoindole and 6,7-dihydro-5H-pyrrolo[3,4-b]pyridine represented by the general formula (I) or salts thereof [wherein B = (un)substituted arom. hydrocarbon or arom. heterocyclic ring optionally contg. 1 or 2 N atom(s); R101, R102, R103 = H, cyano, halo,

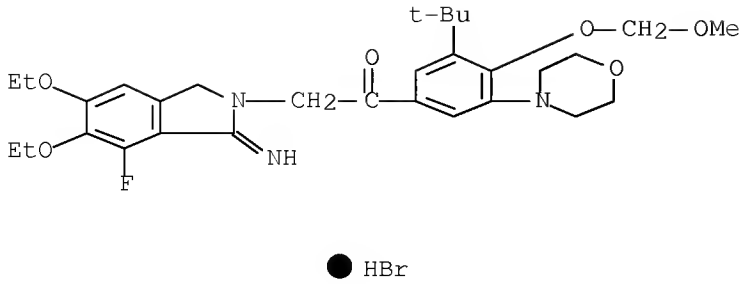
each (un)substituted C1-6 alkyl, C2-8 alkenyl, C2-8 alkynyl, acyl, CO2H, CONH2, C1-6 alkoxycarbonyl, C1-6 alkylaminocarbonyl, HO, C1-6 alkoxy, C3-8 cycloalkyloxy, NH2, C1-6 alkylamino, C3-8 cycloalkylamino, acylamino, ureido, sulfonylamino, sulfonyl, SO2NH2, or C3-8 cycloalkyl, etc.; Y1 = a single bond, (CH2)m, each (un)substituted CH, CH2, NH, CONH, or SO2NH, CH2CO, SO, SO2, CO (wherein m = an integer of 1-3); Y2 = a single bond, O, N, (CH2)m, each (un)substituted CH, CH2, or C(:NOH), CO, SO, SO2; Ar = H, (un)substituted Ph] are prepd. These compds. are thrombin receptor antagonists, in particular thrombin PAR1 receptor antagonists and are useful as blood platelet aggregation inhibitors and proliferation inhibitors of smooth muscle cell, endothelial cell, fibroblast, kidney cell, osteosarcoma cell, muscle cell, cancer cell, and/or glial cell and for the treatment and/or prevention of thrombosis, vascular restenosis, deep vein thrombosis, lung embolism, cerebral infarction, heart disease, disseminated intravascular coagulation syndrome, hypertension, inflammation, rheumatism, asthma, glomerulonephritis, osteoporosis, nerve disease, and/or malignant tumor. Thus, [6-[(1-imino-1,3-dihydroisoindol-2-yl)acetyl]-2,3- dihydrobenz[1,4]oxazin-4-yl]acetonitrile deriv. (II) in vitro showed IC50 of 0.017 .mu.M for inhibiting the binding of [3H]Ala-(4-fluoro)Phe-Arg- (cyclohexyl)Ala-homoArg-Tyr-NH2 to thrombin receptor of human blood platelet, that of 0.29 .mu.M for inhibiting the human blood platelet aggregation induced by thrombin, and that of 0.0061 .mu.M for inhibiting the proliferation of rat smooth cell.

IT 474543-84-5P 474544-04-2P 474544-11-1P
474544-14-4P 474544-63-7P 474550-69-1P
474550-70-4P 474553-86-1P 474631-43-1P
474632-18-3P 474633-46-0P 474639-14-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of dihydroisoindole and dihydro-5H-pyrrolo[3,4-b]pyridine derivs. as thrombin receptor antagonists and remedies and/or preventives for diseases)

RN 474543-84-5 CAPLUS
CN Ethanone, 2-(5,6-diethoxy-7-fluoro-1,3-dihydro-1-imino-2H-isoindol-2-yl)-1-[3-(1,1-dimethylethyl)-4-ethoxy-5-(4-morpholinyl)phenyl]-, hydrobromide (1:1) (CA INDEX NAME)

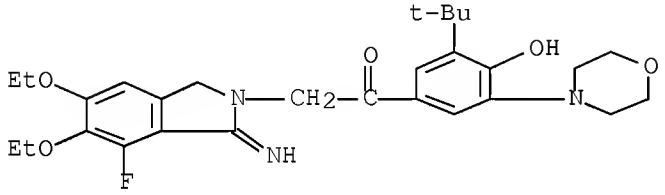



RN 474544-04-2 CAPLUS
CN Ethanone, 2-(5,6-diethoxy-7-fluoro-1,3-dihydro-1-imino-2H-isoindol-2-yl)-1-[3-(1,1-dimethylethyl)-4-(methoxymethoxy)-5-(4-morpholinyl)phenyl]-, hydrobromide (1:1) (CA INDEX NAME)



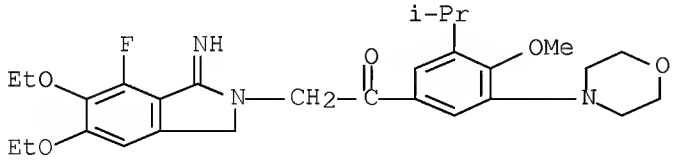
● HBr

RN 474544-11-1 CAPLUS
CN Ethanone, 2-(5,6-diethoxy-7-fluoro-1,3-dihydro-1-imino-2H-isoindol-2-yl)-1-[3-(1,1-dimethylethyl)-4-hydroxy-5-(4-morpholinyl)phenyl]-, hydrochloride (1:1) (CA INDEX NAME)



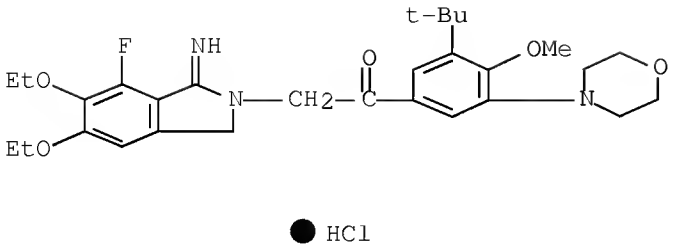
● HCl

RN 474544-14-4 CAPLUS
CN Ethanone, 2-(5,6-diethoxy-7-fluoro-1,3-dihydro-1-imino-2H-isoindol-2-yl)-1-[4-methoxy-3-(1-methylethyl)-5-(4-morpholinyl)phenyl]-, hydrobromide (1:1) (CA INDEX NAME)



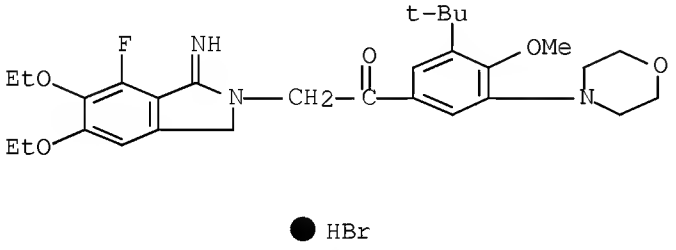
● HBr

RN 474544-83-7 CAPLUS
CN Ethanone, 2-(5,6-diethoxy-7-fluoro-1,3-dihydro-1-imino-2H-isoindol-2-yl)-1-[3-(1,1-dimethylethyl)-4-methoxy-5-(4-morpholinyl)phenyl]-, hydrochloride (1:1) (CA INDEX NAME)



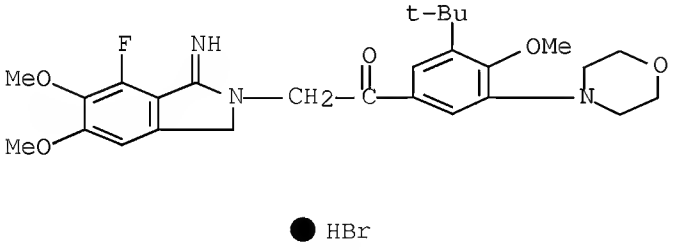
● HCl

RN 474550-69-1 CAPLUS
CN Ethanone, 2-(5,6-diethoxy-7-fluoro-1,3-dihydro-1-imino-2H-isoindol-2-yl)-1-[3-(1,1-dimethylethyl)-4-methoxy-5-(4-morpholinyl)phenyl]-, hydrobromide (1:1) (CA INDEX NAME)



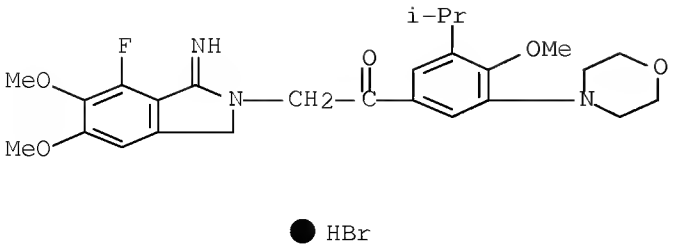
● HBr

RN 474550-70-4 CAPLUS
CN Ethanone, 1-[3-(1,1-dimethylethyl)-4-methoxy-5-(4-morpholinyl)phenyl]-2-(7-fluoro-1,3-dihydro-1-imino-5,6-dimethoxy-2H-isoindol-2-yl)-, hydrobromide (1:1) (CA INDEX NAME)



● HBr

RN 474553-86-1 CAPLUS
CN Ethanone, 2-(7-fluoro-1,3-dihydro-1-imino-5,6-dimethoxy-2H-isoindol-2-yl)-1-[4-methoxy-3-(1-methylethyl)-5-(4-morpholinyl)phenyl]-, hydrobromide (1:1) (CA INDEX NAME)

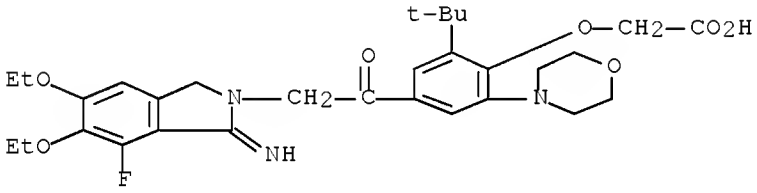


● HBr

RN 474631-43-1 CAPLUS
CN Acetic acid, 2-[4-[2-(5,6-diethoxy-7-fluoro-1,3-dihydro-1-imino-2H-isoindol-2-yl)acetyl]-2-(1,1-dimethylethyl)-6-(4-morpholinyl)phenoxy]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

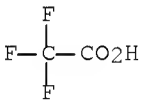
CM 1

CRN 474631-42-0
CMF C30 H38 F N3 O7

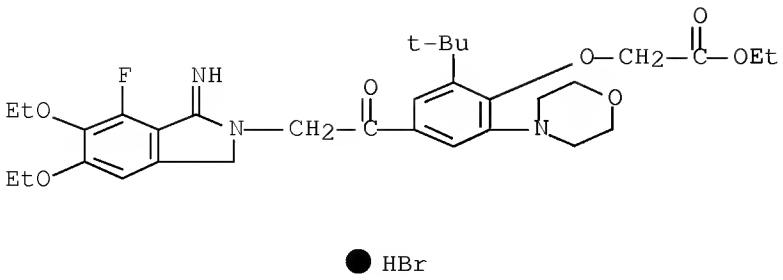


CM 2

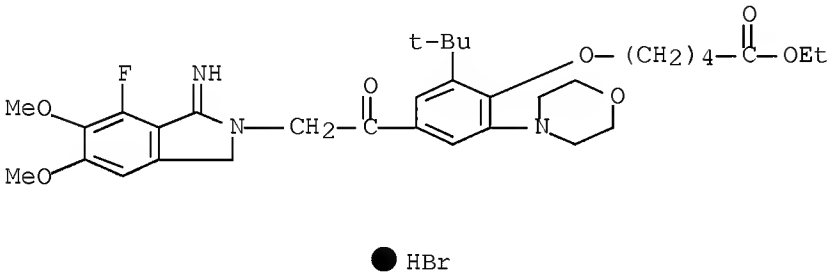
CRN 76-05-1
CMF C2 H F3 O2



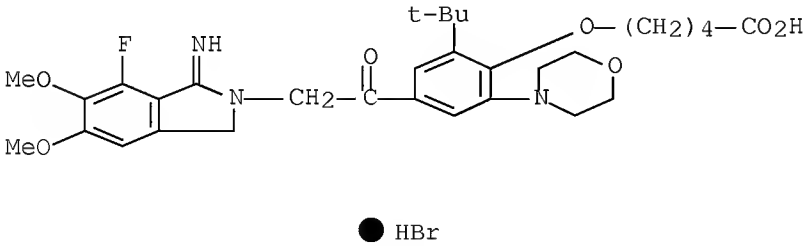
RN 474632-18-3 CAPLUS
CN Acetic acid, 2-[4-[2-(5,6-diethoxy-7-fluoro-1,3-dihydro-1-imino-2H-isoindol-2-yl)acetyl]-2-(1,1-dimethylethyl)-6-(4-morpholinyl)phenoxy]-, ethyl ester, hydrobromide (1:1) (CA INDEX NAME)



RN 474633-46-0 CAPLUS
CN Pentanoic acid, 5-[2-(1,1-dimethylethyl)-4-[2-(7-fluoro-1,3-dihydro-1-imino-5,6-dimethoxy-2H-isoindol-2-yl)acetyl]-6-(4-morpholinyl)phenoxy]-, ethyl ester, hydrobromide (1:1) (CA INDEX NAME)



RN 474639-14-0 CAPLUS
CN Pentanoic acid, 5-[2-(1,1-dimethylethyl)-4-[2-(7-fluoro-1,3-dihydro-1-imino-5,6-dimethoxy-2H-isoindol-2-yl)acetyl]-6-(4-morpholinyl)phenoxy]-, hydrobromide (1:1) (CA INDEX NAME)



REFERENCE COUNT: 100 THERE ARE 100 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 80.62 | 259.19 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| CA SUBSCRIBER PRICE | -11.20 | -11.20 |

STN INTERNATIONAL LOGOFF AT 06:57:34 ON 14 JUN 2008